5. (NEW) A recombinant expression vector comprising the isolated nucleic acid molecule of claim 3.

6. (NEW) A host cell comprising the recombinant expression vector of claim 5.

7. (NEW) A recombinant expression vector comprising the isolated nucleic acid molecule of claim 4.

8. (NEW) A host cell comprising the recombinant expression vector of claim 7.

RESPONSE

I. Status of the Claims

Claims 5-8 have been added. Applicants submit that Claims 5-8 are dependent claims that are properly classified into the same class and subclass and are therefore proper. Claims 1-8 are therefore presently pending in the case. For the convenience of the Examiner, a clean copy of the pending claims is attached hereto as **Exhibit A**. In compliance with 37 C.F.R. § 1.121(c)(1)(ii), a marked up copy of the original claims is attached hereto as **Exhibit B**.

II. Support for the Amended Claims

Claim 5 has been added to specifically recite recombinant expression vectors comprising the isolated nucleic acid molecule of Claim 3. Support for this claim can be found throughout the specification and in claim 1 as originally filed, with particular support being found in at least at page 17, lines 10-14.

Claim 6 has been added to specifically recite host cells comprising the recombinant expression vectors of claim 5. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least at page 17, lines 14-17.

Claim 7 has been added to specifically recite recombinant expression vectors comprising the isolated nucleic acid molecule of Claim 4. Support for this claim can be found throughout the specification and in claim 1 as originally filed, with particular support being found in at least at page 17, lines 10-14.

Claim 8 has been added to specifically recite host cells comprising the recombinant expression vectors of claim 7. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least at page 17, lines 14-17.

As new claims 5-8 are fully supported by the specification and claims as originally filed, they do not constitute new matter. Entry, therefore, is respectfully requested.

III. Rejection of Claims Under 35 U.S.C. § 101

The Action persists in rejecting claims 1-4 under 35 U.S.C. § 101, allegedly because the claimed invention lacks support by either a specific and substantial asserted utility or a well established utility. Applicants respectfully continue to traverse.

The present application describes a novel G-protein coupled receptor. Of the pharmaceutical products currently being market by the entire industry, 60% of these drugs target G-protein coupled receptors (Gurrath, 2001, Curr. Med. Chem. *8*:1257-1299). Given that more than half of the currently marketed drugs target proteins that are structurally (7TM proteins) and functionally (G-protein interaction) related to the presently described sequences, a preponderance of the evidence clearly weighs in favor of Applicants' assertion that the presently described sequences have a specific (the claimed GPCR proteins are encoded by a specific locus on the human genome), credible, and well-established utility.

The Action quotes several articles, for example, one by Ji *et al.* ("Ji"; 1998, J. Biol. Chem. *273*:17299-17302) as teaching that structural homology alone is not a good predictor of function. But an exact quote from Ji, completely undermines this argument: "a substantial degree of amino acid homology is found between members of a particular subfamily, but comparisons between subfamilies show significantly less or no similarity" (Ji at 17299, first paragraph, emphasis added). This quote suggests that homology with members of a G-protein coupled receptor is indicative that the particular sequence is in fact a member of that subfamily - the fact that there is little or no homology between subfamilies is completely irrelevant.

The Action also cites Yan *et al.* ("Yan"; 2000, Science 290:523-527) for the proposition that "even a two-amino acid substitution in a molecular structure of a protein can lead to total loss of a protein (*sic*) to bind a specific receptor" (Action at page 4). However, this paper cites only one example, two isoforms of the anhidrotic ectodermal dysplasia (EDA) gene, where a two amino acid change conforms one isoform (EDA-A1) into the second isoform (EDA-A2). However, while it is true that this amino acid change results in binding to different receptors, it is important to note that the different receptors bound by the two isoforms are in fact related (Yan at page 523). Furthermore, the EDA-A2 receptor was correctly identified as a member of the tumor necrosis factor receptor superfamily based solely on sequence similarity (Yan at page 523). Thus, Yan is hardly indicative of a high level of uncertainty in assigning function based on sequence, and thus also does not support the alleged lack of utility.

Rather, as set forth by the Federal Circuit, "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that to violate § 101 the claimed invention "must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985)) states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Id* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

The Action states that commercial success is not an indication of patentability (page 4, line 14-15) and that "For example, a pharmaceutical company may wish to purchase a putative G-protein coupled receptor on the chance that it may turn out to be a drug target in the future"(page 4, line 16-18). It is hard to accept that a pharmaceutical company, or for that matter any company, would expend limited assets and resources to purchase a potential drug target, unless that target had a well recognized and generally accepted utility. The Action points out that identification of the ligand for any such receptor may require substantial further experimentation. It may, and certainly being in possession of the ligand to your receptor increases the potential value of any deal, but a ligand is likely a distinct

invention and its presence or absence does not detract from the value and utility of the receptor. Indeed, agonists and antagonists can and have been developed without knowledge of the natural ligand for a receptor.

The Action argues (on page 5, lines 11-12) that " Without knowing biological function of the claimed molecule, would not know what to do with the claimed invention." In fact the biological function of the claimed invention has been disclosed, it is a GPCR and has the biological functions know to those of skill in the art of GPCRs. Indeed, it is difficult to accept the given the propensity of knowledge surrounding GPCRs, in published articles and books, issued patents and the like, that one of skill in the art would not know what to do with the claimed invention and would not readily recognize its utility. Thus, for the many reasons laid out above and including those of the earlier response (Paper 7) the Examiner is respectfully requested to withdraw the pending rejection of Claims 1-4 under 35 U.S.C. § 101.

IV. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

The Action rejects claims 1-4 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the claimed invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as claims 1-4 have been shown to have a specific, substantial, credible and well established utility (see above) and that given the identification of the present invention as a GPCR and the related disclosures, the wealth of published art, as well as issued U.S. Patents on the utility and use of GPCRs and combined the disclosure of the present invention, those of skill in the art would clearly know how to make and use the present invention without undue experimentation. Applicants therefore respectfully request that the rejection of claims 1-4 under 35 U.S.C. § 112, first paragraph, be withdrawn.

V. Rejection of Claim 2 Under 35 U.S.C. § 112, Second Paragraph

The Action rejects Claim 2 as allegedly indefinite based on the use of phrase " highly stringent conditions". As the specification provides specific teaching regarding "highly stringent hybridization conditions", at least at page 7, lines 21-27, Applicants submit that as revised Claim 2 clearly meets the

requirements of 35 U.S.C. § 112, second paragraph. Applicants stress that "a claim need not 'describe' the invention, such description being the role of the disclosure". *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). Based on the foregoing, Applicants submit that Claim 2 is sufficiently definite, and therefore respectfully request withdrawal of this rejection

VI. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Li have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

This response is timely filed and Applicants believe no fees are due in connection with this response. However, should this be incorrect the Commissioner is authorized to charge any required fees or credit any overpayment to Deposit Account No. 50-0892.

Respectfully submitted,

July 12, 2002
Date

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PATENT TRADEMARK OFFICE

Exhibit B

Marked Up Version of Amended Claims in U.S. Patent Application Ser. No. 09/775,181

1. (Amended) An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1.

2. (Amended) An isolated nucleic acid molecule comprising a sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO: 2; and

(b) hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof.

3. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO: 2.

4. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO:4.

5. (NEW) A recombinant expression vector comprising the isolated nucleic acid molecule of claim 3.

6. (NEW) A host cell comprising the recombinant expression vector of claim 5.

7. (NEW) A recombinant expression vector comprising the isolated nucleic acid molecule of claim 4.

8. (NEW) A host cell comprising the recombinant expression vector of claim 7.